REMARKS

The Office Action and the cited and applied references have been carefully reviewed. No claim is allowed. Claim 127 presently appear in this application and defines patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claim 124 and 125 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Nakamura et al., *Infect. Immun*. 61:64-70 (1993), and Campbell and further in view of Shulman et al., *Nature* 276:269-270 (1978) and claim 126 has been rejected under 35 U.S.C. §103(a) as being unpatentable over the same Nakamura, Campbell and Shulman references and further in view of Numata et al., US 5,358,850.

Both of the above §103(a) rejections are obviated by the cancellation of claims 124-126 without prejudice.
New claim 127 is added in place of cancelled claims 124-126. Support for new claim 127 is found in the present specification at page 19, first full paragraph, pages 49-50 (Examples 5-1 and 5-2), and pages 50-52 (Example 6). Example 5-2 in particular discloses that crude IGIF or IL-18 containing IGIF or IL-18 and impurities was purified by immunoaffinity chromatography using the claimed monoclonal antibody to obtain IGIF or IL-18 with a

purity of 95% or more in a yield of nearly 100% of the original material.

The fact that IGIF or IL-18 with a purity of 95% or more was obtained by immunoaffinity chromatography using the presently claimed monoclonal antibody in a yield of nearly 100% of the original material implicitly means that the claimed monoclonal antibody substantially adsorbs IGIF or IL-18 but does not substantially adsorb proteins other than IGIF or IL-18. In other words, the monoclonal antibody is an antibody very specific for IGIF or IL-18.

Similarly, Example 6 discloses that crude IGIF or IL-18 containing IGIF or IL-18 and impurities was purified by immunoaffinity chromatography using the presently claimed monoclonal antibody to obtain IGIF or IL-18 with a purity of 95% or more in a yield of nearly 100% of the original material. This example also implicitly supports the language of new claim 127 and the monoclonal antibody being an antibody very specific for IGIF or IL-18.

The teachings of the Nakamura reference relied upon by the examiner have been set forth in previous Office Actions. The examiner has taken the position that it would have been obvious at the time the invention was made to obtain a monoclonal antibody of the present invention by using the

"factor" disclosed in Nakamura as antigen and by using hybridoma methodology for producing monoclonal antibodies as is well known in the art.

Insofar as the presently claimed monoclonal antibody is concerned, submitted herewith is a 1.132 declaration executed by Dr. Tsunetaka Ohta (an expert in the art of IGIF/IL-18 with many publications relating to IGIF/IL-18) explaining why the presently claimed monoclonal antibody is not obvious over Nakamura. As explained in the declaration, the first reason is that those of ordinary skill in the art would not have been motivated to obtain a monoclonal antibody which binds "Nakamura's Factor" and the second reason is that, even if those of ordinary skill in the art were to seek such a monoclonal antibody, they would have met with failure because obtaining sufficient quantities of the "factor" from mice to generate monoclonal antibodies thereto is just an enormous undertaking involving undue experimentation beyond the normal capacity of those of ordinary skill in the art.

Furthermore, it should be noted that the monoclonal antibody of new claim 127 is not only a monoclonal antibody which simply recognizes IGIF or IL-18, but it is also a monoclonal antibody which has quite high binding (adsorbing) ability to IGIF or IL-18, and therefore it has quite high

specificity and affinity to IGIF or IL-18. Applicants believe it would not have been obvious to one ordinary skill in the art to obtain such monoclonal antibody, even though the hybridoma method had been known at the invention was made as a method for preparing a monoclonal antibody against an antigen, because it would have been impossible to judge if a monoclonal antibody thus obtained would specifically bind to IGIF or IL-18 without first obtaining a purified and isolated IGIF or IL-18. Applicants therefore believe that there is nothing in Nakamura as well as in any other publications cited by the examiner in the prosecution of the instant application that would teach or suggest the monoclonal antibody as defined in new claim 127.

In addition, it should be noted that the present inventors discovered that it is mouse liver cells that produce IGIF or IL-18, and succeeded in obtaining IGIF or IL-18 through recombinant DNA technology using mRNA isolated from the mouse liver cells in an amount necessary and sufficient for preparing a monoclonal antibody specific for IGIF or IL-18. Without such technical breakthroughs, which are not trivial, it would have been impossible to obtain the monoclonal antibody of the present invention. This was stated by Dr. Okamura, one of the present inventors, in his 1.132 Declaration filed September 24, 2009, at page 6-7, paragraph "9. Breakthrough".

Accordingly, Nakamura alone or in combination with any cited and applied reference of record cannot make obvious the presently claimed invention.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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Appendix

The Appendix includes the following item(s):

- Executed 1.132 Declaration with CV and cited reference